

REMARKS

Upon entry of the present amendment, claims 1-4, 6, 10-14, 19, 29, 31, and 35-43 are pending in the application, claims 5, 7-9, 15-18, 20-28, 30, and 32-34 having been canceled by the present amendment.

Claims 1, 3, 4, 14 and 19, are amended herein to reflect more accurately reflect the invention. For example, claim 1 has been amended to require the first domain of the chimeric polypeptide to comprise the intracellular portion of a GPCR, and to lack an extracellular portion of a GPCR. Support for this amendment can be found in the application and claims as originally filed. Claim 3 has been amended to recite that the hydrophobic moiety is a lipid. Support for this amendment can be found in the application and claims as originally filed. Claim 4 has been amended to correct antecedent basis in view of the amendment to claim 3, to correct typographical errors relating to the number of carbons in each hydrophobic moiety, and to include steroyl and lauryl lipid moieties. Support for this amendment can be found in the application and claims as originally filed, *see*, for example, pages 3 and 16. Claim 14 has been amended to recite that the chimeric polypeptide of claim 1 includes a first domain which comprises a PAR and a second domain which comprises a lipid moiety. Claim 19 has been amended to correct its dependency.

Claims 35-43 have been added. Claim 35 corresponds to former claim 18 which, due to a typographical error, was drawn to a nucleic acid instead of a chimeric polypeptide of the invention, and, thus was subjected to restriction. Support for new claims is found in the application and claims as originally filed. *See*, for example, pages 3 and 16 of the specification, discussing hydrophobic moieties and Figures 2A, 6A, and Table 1, listing various sequences of the invention.

The specification was amended to correct typographical errors on pages 9-10, and pages 43 and 46 were corrected to remove URL's.

No new matter has been added.

I. Informalities

The disclosure was objected to because it contained URL's. Pages 43 and 46 were corrected to remove reference to browser-executable code.

II. Claim Objections

Claims 3, 4, 8, and 19 were objected to for reciting non-elected inventions (*e.g.*, "ceramides" or "VIP" receptors).

Claim 8 has been cancelled herein. Therefore, the objection should be withdrawn with respect to this claim.

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Applicants submit that claims 3, 4, and 19 are not drawn to unelected inventions, and that objection to unelected species is improper. Claim 3, as amended herein, requires the hydrophobic moiety to be a lipid. In response to a restriction requirement/species election (paper 14) mailed February 28, 2003, Applicants elected the species palmitate, an example of a lipid. Claim 4, as amended herein, presents a list of lipid species, which are used in the hydrophobic moieties of the chimeric polypeptides of the invention. Claim 19 recites species of GPCRs from which the intracellular portion of the chimeric polypeptides of the invention can be derived. In response to a restriction requirement/species election (paper 14) mailed February 28, 2003, Applicants elected the species protease-activated receptor (PAR).

Claim 3 recites a generic hydrophobic moiety, lipid, and claim 4 recites a Markush group of lipids, of which palmitate is a species. Claim 19 recites a Markush group of GPCRs of the invention, of which PAR is a species. As such, Applicants respectfully submit that the lipids and GPCRs recited in these claims share a common utility.

“Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.” MPEP § 803.02

Further, MPEP § 803.02 states that ... “should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended.... The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim.”

Since no prior art was found to be relevant to the patentability of the PAR and palmitate species, Applicants respectfully request the search of members of the Markush group be extended and that the objection to claims 3, 4, and 19 be withdrawn.

III. Rejections under 35 U.S.C. §112, first paragraph

A) Enablement

Claims 1-17, 19-21, 29 and 31 were rejected for overbreadth and lack of enablement. The Examiner states:

The specification, while enabling for a pepducin constructed from the third intracellular loop of the PAR4 receptor, comprising...(SEQ ID NO:9) and

attached to a fatty acid such as palmitate, does not reasonably provide enablement for chimeric peptides comprising portions of G-protein coupled receptors other than PAR4, or of the extracellular domains of such G-protein coupled receptors, or of pepducins attached to hydrophobic moieties other than fatty acids such as palmitate.

Office Action at Page 4. Claims 5, 7-9, 15-17, and 20-21 have been canceled herein. Thus, the rejection as it applies to these claims is moot and should be withdrawn.

Independent claim 1, and the corresponding dependent claims, have been amended to require that the first domain of the chimeric polypeptide comprise intracellular portions of a G-protein coupled receptor. Thus, the aspect of the rejection relating to extracellular domains of G-protein coupled receptors is moot and can be withdrawn.

Section 112, first paragraph, requires that the specification provide a description that, when coupled with the knowledge possessed by a person of ordinary skill in the art, enables that person to make and use the claimed invention. Atlas Powder Co. v. E.I. duPont De Nemours & Co., 750 F.2d 1569, 1576 (Fed. Cir. 1984). Enablement is not precluded by the necessity for some experimentation; however, any required experimentation must not be undue experimentation. In re Wands, 858 F.2d 731, 736-7 (Fed. Cir. 1988).

The MPEP states that there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." Factors to be considered include (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. MPEP at 2164.01(a); In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Applicants submit that, in weighing all eight factors, the specification meets the standard for enablement for the full scope of the claimed invention.

The breadth of the claims

The claims have been amended to require that the first domain of the chimeric polypeptide comprises an intracellular portion of a GPCR and a hydrophobic moiety. Thus, the amended claim does not encompass an extracellular portion of a GPCR, and requires that the polypeptide does not include a native extracellular portion of the GPCR.

These critical limitations exclude native GPCR ligands by specifying a structural requirement (*i.e.*, that the GPCR portion is an intracellular portion) and by requiring attachment of a hydrophobic moiety to the GPCR (first) domain.

Claims 6 and 10-13 further define the intracellular portion of the GPCR. Claim 3 requires that the hydrophobic moiety be a lipid, and claim 4 and (new) claims 36 and 42 specify particular types of lipids.

Claim 14 requires that the first (GPCR) domain is a PAR, and that the second (hydrophobic) domain is a lipid.

Claim 19 also recites the types of GPCRs to be used in the invention, and claim and 37 requires that the GPCR of claim 19 is a PAR. Claim 38 specifies that the PAR of claim 37 is PAR1, PAR2, or PAR4. Claims 39-40 specify specific sequences of the GPCR moiety.

The claims are commensurate with Applicants' discovery, and the specification provides sufficient guidance to carry out the claimed methods to the full extent of their scope.

The nature of the invention and State of the prior art

These factors are not explained in Wands, but it might be reasonable to assume that the court was referring to the foundation in the art for the claims and the advance represented by the claims. The nature of the invention is novel pepducins: chimeric polypeptides which comprise a GPCR moiety and a hydrophobic moiety.

Applicants have made an important contribution to the field of GPCR agonists and antagonists by describing a number of compositions, *i.e.*, pepducins, which disrupt G-protein-receptor interaction and cause activation or inhibition of signalling. Exploitation of this discovery according to the amended claims allows specific targeted modulation of G-protein receptor signalling by selecting a pepducin specific for that GPCR -- by determining the optimum GPCR moiety and hydrophobic moiety. Thus, the claims represent a significant advance in the field of inhibition of GPCR signalling.

The level of one of ordinary skill in art

Applicants submit that the level of skill of those skilled in the field of agonism and antagonism of GPCR signalling is very high. Skilled artisans have been practicing in the field GPCR signalling for many years. Accordingly, armed with the information provided in the specification regarding which GPCR to choose, which intracellular GPCR moiety to select, and what kind hydrophobic moiety to select, and how to combine the selected GPCR and hydrophobic moieties to produce the pepducins of the invention. Those skilled in the art would

readily be able to carry out the invention as now claimed. Undue experimentation would not be required for one skilled in the art to carry out the invention claimed by amended claim 1, new claim 43, and those claims which depend from claims 1 and 43.

Predictability or unpredictability of the art

With respect to the this factor, the Examiner indicates that the “unpredictability of function based on structural similarity of proteins” would require undue experimentation on the part of a skilled artisan to make and use the claimed invention in its full scope. *See* Office Action at page 5.

The amended claims require that the chimeric polypeptide comprise a first domain which includes an intracellular portion of a GPCR but does not include an extracellular portion of the GPCR, and a second domain which includes a hydrophobic moiety. The data presented in the specification and the accompanying Declaration of Dr. Athan Kuliopoulos (Exhibit A) indicate that the claimed functional pepducins derived from intracellular portions of a GPCR are reliably and consistently generated by a skilled artisan using the techniques provided in the specification. The only reason given by the Examiner for the alleged unpredictability of the invention is a general reason pertaining to potential problems associated with using protein structure alone to select GPCR moieties. For example, Claim 14 requires that the first domain of the chimeric peptide be a protease activated receptor (PAR) and the second domain be a lipid moiety. The specification is replete with examples of intracellular loop domains of PAR 1 attached to a lipid. The Declaration of Dr. Kuliopoulos provides additional evidence regarding the predictability of the claimed constructs. There is no reason to believe that pepducins derived from intracellular portions of a GPCR, as now claimed, would not lead to chimeric polypeptides when coupled with a hydrophobic moiety.

The amount of direction or guidance presented

The greater the amount of guidance provided, the more this factor weights in favor of granting the claim.

The specification of the present application provides ample guidance regarding the procedures required to carry out the generation of functional chimeric polypeptides of the invention which specifically target and agonize/antagonize G-protein receptor signalling. For example, a proposed mechanism for pepducin activity is presented in Figure 4E, as discussed at page 11 of the specification. Chimeric and fusion peptides of the invention are described, at least, at page 16, line 4 - page 17, line 2, and in Examples 1 and 4 of the specification. Methods

of assaying pepducins are described in Examples 2, 3 and 6, of the specification. Determination of which regions of the GPCR interact with the pepducins are described in Example 5.

For example, the specification teaches how to make and evaluate PAR/lipid constructs, e.g., PAR1, PAR2, and PAR4 polypeptides. Table 1 lists, and provides data from the testing of, pepducins generated from PAR1, PAR2, PAR4, SSTR2, CCKA, and CCKB. See, for example, page 12, lines 7 - page 13, line 10, and, e.g., Example 4. Example 8 also describes pepducin modulation of the MC4 obesity receptor.

Thus, Applicants submit that adequate guidance is provided in the specification of the application to allow one skilled in the art to carry out the claimed invention without undue experimentation.

The existence of working examples

The specification presents several examples of pepducins generated from various GPCRs. For example, Table 1 lists, and provides data from the testing of, pepducins generated from PAR1, PAR2, PAR4, SSTR2, CCKA, and CCKB. See, e.g., Table 1, also, page 12, lines 7 - page 13, line 10, and, e.g., Example 4. Example 8 also describes pepducin modulation of the MC4 obesity receptor.

Furthermore, the Examiner indicates that the specification is enabled for pepducins prepared from PAR4 peptides (Office Action at page 3), however the specification discloses several examples of the synthesis and testing of pepducins generated from PAR1, PAR2, and PAR4. See, e.g., Figures 2A, 2B - 2G, 4A - 4D, 6A-6B, 6D, Table 1, page 12, lines 7- page 13, line 10, and e.g., Examples 4 and 6.

The Examiner has cited Coughlin *et al.*, 2003, *J. Clin. Invest.*, 111(1):25-27 (“Coughlin”) to illustrate the number of types of proteins which can be generated from portions of GPCRs (Office Action at page 4). However, Coughlin deals exclusively with the PAR subclass of GPCRs, and indicates that there are four PARs currently known (page 25, middle column). Applicants have made and tested pepducins based on three of four of them.

With respect to the hydrophobic moiety element of the claims, Applicants present additional data summarizing the preparation and testing of various pepducins comprising a GPCR peptide coupled to a number of different hydrophobic moieties: such as fatty acid or steroid lipids. In the accompanying Declaration of Dr. Athan Kuliopoulos (Exhibit A), an expanded panel of pepducins was tested for the ability to antagonize SFLLRN-induced human platelet aggregation (Figure E), and as inhibitors of human platelet aggregation (Figure F). Also, data in Exhibit A shows that the agonistic effect of PAR1 i3 loop pepducins P1pal-19 and P1pal-13 is not dependent on the presence of palmitate.

The data described in the specification and in of Dr. Kuliopoulos' declaration indicate that PAR1 i3 loop-based peptide myristic, palmitic, cholanic, lithocholic, cholic, and lauric, derivatives, along with PAR4 P4-10 cholanic, lithocholic, palmitic, myristic, and stearic derivatives are capable of inhibiting platelet aggregation. This inhibitory activity is not limited to PAR4, nor is it limited to palmitate. The data described in the specification and Dr. Kuliopoulos' declaration also shows that the stimulatory effect on platelet aggregation shown by P1pal-19 and P1pal-13 is not limited to palmitate, but also is effective when these shortened PAR1 peptides are linked to lithocholate, myristate, deoxycholate, cholate, caprylate, or laurate.

The quantity of experimentation necessary

In Wands, the Court stated,

[A] considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Applying this criterion here, all of the techniques required to practice the claimed methods were described in the specification or were well-known to those skilled in the art as of the filing date. For example, little or no experimentation is required to choose a particular PAR, and determine which intracellular moiety and which hydrophobic moiety to select, and how to couple them. Since extensive guidance is provided regarding examples of selection of intracellular moieties from various GPCRs, and of particular hydrophobic moieties, minimal experimentation would be required to couple the two domains to arrive at the chimeric polypeptides of the invention. Although some experimentation may be required to determine the exact length of GPCR moiety to be used, such determinations are routine in the art and would not require undue experimentation.

Applicants submit that the specification coupled with the knowledge in the art of peptide synthesis fulfills the requirements of §112 and that the skilled practitioner would not have to resort to undue experimentation to practice the claimed invention. Applicants therefore request withdrawal of the rejection of claim 1 and dependent claims 2-4, 6, 10-14, 19, 29, and 31.

B) Written Description

Claims 1-17, 19-21, 29 and 31 were rejected for lack of written description. Claims 5, 7-9, 15-17, and 20-21 have been canceled herein. Thus, the rejection as it applies to these claims is moot and should be withdrawn.

The Examiner states that, "the description of several polypeptides attached to fatty acids is not adequate written description of an entire genus of functionally equivalent polypeptides attached to any lipid." Applicants traverse.

The Revised Interim Written Description Guidelines provide a framework for analyzing whether or not a genus meets the statutory requirements for written description:

- 1) Determine whether the art indicates substantial variation among the species within the genus of the claimed subject matter.
- 2) Is there a representative number of species implicitly or explicitly disclosed? What is a representative number of species depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes of features of the elements possessed by the members of the genus in view of the species disclosed or claimed?

If the answers to the questions in part two of the analysis are yes, then the claim meets the written description requirement; if the answers are no, then it doesn't.

GPCRs

Applicants submit that the written description requirement has been fulfilled for the GPCR genus required by amended independent claim 1 and dependent claim 19, and indeed, for the PAR genus required by dependent claims such as claims 14, and new claims 37-38, 40 and 43.

Part one of the written description analysis addresses the level of variation of species within a genus. GPCRs are a well-defined family of proteins known in the art. Family members share the following structural attributes: GPCRs are cell surface molecules that cross a cell membrane at least once (and thus contain at least one intracellular domain). Many GPCRs share a seven transmembrane domain structure in common with many neurotransmitter and hormone receptors. The structure of these receptors is likely to underlie the recognition and G-protein-mediated transduction of various signals. Human GPCRs generally do not contain introns and belong to four different gene subfamilies, displaying great sequence variability. *See, e.g.,* Online Mendelian Inheritance in Man (OMIM) (<http://www.ncbi.nlm.nih.gov/entrez/ dispomim.cgi>) entry # 164342.

The members of the genus also share the following functional attributes. A GPCR binds to a signaling molecule and mediates the transmission of intracellular signals by activating guanine nucleotide-binding proteins (G proteins) to which the receptor is coupled. Binding of a specific signaling molecule to the GPCR causes a conformational change in the receptor, resulting in a form that is able to bind and activate a G protein, thereby triggering a cascade of

intracellular events that eventually leads to a biological response. Typically, GPCRs interact with G proteins to regulate the synthesis of intracellular second messengers such as cyclic AMP, inositol phosphates, diacylglycerol and calcium ions. Thus, substantial similarity exists between the species within the claimed genus.

A representative number of species are explicitly disclosed in the originally-filed specification. See, *e.g.*, Table 1, also, page 12, lines 7 - page 13, line 10, and, *e.g.*, Example 4. Example 8 also describes pepducin modulation of the MC4 obesity receptor. Moreover, three out of four known species of the subgenus PAR are disclosed at Figures 2A, 2B - 2G, 4A - 4D, 6A-6B, 6D, Table 1, page 12, lines 7- page 13, line 10, and, *e.g.*, Examples 4 and 6.

Additional members of the genus are implicitly disclosed. The presence of identifiable domains in GPCR proteins, is determined by searches using software algorithms such as PROSITE, DOMAIN, Blocks, Pfam, ProDomain, and Prints, and then determining the Interpro number by crossing the domain match (or numbers) using the Interpro website (<http://www.ebi.ac.uk/interpro>). Such data indicates whether the putative GPCR sequence has properties similar to those of other proteins known to contain this domain as well as to the prototypical GPCR domain, the seven transmembrane receptor (rhodopsin family) fragment" (7tm_1 domain) itself. The 7 transmembrane receptor family includes a number of very different types of proteins which are nonetheless structurally related, including, for example, serotonin receptors, dopamine receptors, histamine receptors, adrenergic receptors, cannabinoid receptors, angiotensin II receptors, chemokine receptors, opioid receptors, G-protein coupled receptor (GPCR) proteins, olfactory receptors (OR), and the like. Some proteins and the Protein Data Base Ids/gene indexes include, for example: rhodopsin (129209); 5-hydroxytryptamine receptors; (112821, 8488960, 112805, 231454, 1168221, 398971, 112806); G protein-coupled receptors (119130, 543823, 1730143, 132206, 137159, 6136153, 416926, 1169881, 136882, 134079); gustatory receptors (544463, 462208); c-x-c chemokine receptors (416718, 128999, 416802, 548703, 1352335); opsins (129193, 129197, 129203); and olfactory receptor-like proteins (129091, 1171893, 400672, 548417).

Therefore, there is little variation among the species of the GPCR genus as required by claim 1 and dependent claim 19. Dependent claims 14, and new claims 37-38, 40 and 43 require that the GPCR be a PAR. Protease activated receptors (PARs) are another well-defined family of proteins, and a subset of the GPCR family. PAR family members share the following structural and functional elements: PARs are seven transmembrane domain GPCRs which are activated by proteolysis of the N-terminal exodomain, which creates a new N-terminus which serves as a tethered ligand which binds intramolecularly to itself to effect transmembrane signalling. See, Coughlin, p.25, column 1. All four known PARs are activated by a serine protease to initiate the intramolecular ligand-activation mechanism. See Andrade-Gordon *et al.*, PNAS 96 (22):12257-

12262 (1999), attached hereto as Exhibit B. Thus, there is substantial similarity among the species of the claimed genus GPCRs, and even less variation with the subgenus PAR, and a representative number of species within the genus have been described in detail in the specification.

Hydrophobic moieties

With respect to the level of variation of species within the genus of hydrophobic moieties, Applicants submit that the written description requirement has been fulfilled for the hydrophobic moiety genus required by amended independent claim 1, and indeed, for the lipid moiety genus required by dependent claims such as claims 3, and 4, and new claims 36, 42 and 43.

Hydrophobic moieties are a well-defined family of compounds known in the art which share several structural and functional attributes. Hydrophobic species, or hydrophobes, are generally electrically neutral and nonpolar, and thus prefer other neutral and nonpolar solvents or molecular environments. As is well known in the art, hydrophobic is often used interchangeably with "oily" or "lipophilic". Hydrophobic (water hating) molecules are nonpolar and cannot form H-bonds with H₂O, therefore they are insoluble in H₂O. Hydrophobic molecules aggregate together in avoidance of H₂O molecules. This attraction/repulsion is known as the hydrophobic (fear of water) force. Hydrophobic molecules can move in and out of cells by passing through lipid bilayers. Common examples of biologically relevant hydrophobic moieties include certain amino acids, lipids and steroids.

Therefore, there is little variation among the species of the hydrophobic moiety genus as required by claim 1, dependent claims 3 and 4, and new claim 42. Dependent claim 3 requires that the hydrophobic moiety be a lipid, dependent claim 4 requires that the lipid be a fatty acid, and new claim 42 specifies that the lipid is a steroid. New claim 36 specifies that the lipid is palmitate.

Lipids are a well-defined family, or subgenus, of hydrophobic moieties. Lipid family members share several structural and functional elements. Lipids are a group of biological substances made up primarily or exclusively of nonpolar groups. As such, lipids typically dissolve more readily in nonpolar solvents than in water. This solubility characteristic is common to the genus and is of extreme importance in cells, because lipids associate into nonpolar groups and barriers, as in the cell membranes that form boundaries between and within cells.

Thus, there is substantial similarity among the species of the claimed genus hydrophobic moieties, and even less variation with the subgenus lipid.

The second part of the written description analysis addresses whether the specification describes a representative number of species within the genus and whether or not (in view of the disclosed species), one of skill in the art would deem the Applicants to be in possession of the invention.

As is discussed above, chimeric polypeptides generated from various GPCRs such as PAR1, PAR2, PAR4, SSTR2, CCKA, and CCKB were described in the specification. With respect to the PAR genus, Applicants describe the claimed construct with essentially every species of the PAR genus. Given the number of species disclosed and the level of variation among the species in the disclosed genus, Applicants submit that the written description requirement has been met with respect to the GPCR genus and the PAR genus.

Moreover, given the copious description of hydrophobic moieties, and in particular, the lipid genus, one of skill in the art would recognize that Applicants were in full possession of the invention with respect to the genus of hydrophobic moieties and the genus of lipids. For example, phospholipids, steroids, sphingosines, ceramides, octyl-glycine, 2-cyclohexylalanine, benzoylphenylalanine, and the fatty acid moieties propionoyl (C₃); butanoyl (C₄); pentanoyl (C₅); caproyl (C₆); heptanoyl (C₇); capryloyl (C₈); nonanoyl (C₉); capryl (C₁₀); undecanoyl (C₁₁); lauroyl (C₁₂); tridecanoyl (C₁₃); myristoyl (C₁₄); pentadecanoyl (C₁₅); palmitoyl (C₁₆); phtanoyl ((CH₃)₄); heptadecanoyl (C₁₇); stearoyl (C₁₈); nonadecanoyl (C₁₉); arachidoyl (C₂₀); heicosanoyl (C₂₁); behenoyl (C₂₂); trucisanoyl (C₂₃); and lignoceroyl (C₂₄); are shown in the specification from page 3, line 23, to page 4, line 4. Thus, hydrophobic moieties described include phospholipids, steroids, and sphingosines, which are lipids but not fatty acids. The fatty acid genus varies only by the number of carbons in the hydrocarbon chain.

Therefore, with respect to claims 1-4, 6, 10-14, 19, 29 and 31, Applicants submit that the specification describes far more than a representative number of examples, indicating that Applicants were in full possession of the claimed genus.

Examiner further also states in the Office Action that one of ordinary skill in the art would not know how to make or use the lipids described in the list above. (*See* Office Action page 6). As shown, for example, in Exhibit A, one of ordinary skill in the art was indeed able to envision the detailed chemical structure of the encompassed polypeptide/lipids, and therefore, knew how to make and use them. Moreover, as disclosed above, the fatty acid genus varies only by the number of carbons in the hydrocarbon chain. The written description in the application as filed is adequate for the entire genus.

Thus, in view of the description of multiple species by physical/structural characteristics, Applicants submit that the specification fulfills the requirements of the statute for written

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description of the genus defined by claims 1-4, 6, 10-14, 19, 29 and 31. Withdrawal of this rejection is respectfully requested.

CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance.

A check in the amount of \$55.00, is enclosed to cover the petition fee for a one (1) month extension of time pursuant to 37 C.F.R. § 1.17(a)(1). With the extension, this response is on or before January 30, 2004.

The Commissioner is hereby authorized to charge any additional fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 18475-034.

Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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